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EDUCATIONAL ARTICLE

Management of Obesity in Patients with Peripheral Arterial Disease

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Obesity is a major risk factor for cardiovascular disorders, including peripheral arterial disease. This review outlines the evidence for a 6-step process for the management of obesity, starting with identifying the degree and type of obesity, followed by target setting, life style and behavioural changes, imposed hypocaloric diet and physical activity, pharmacological treatment and consideration of eating disorders and/or bariatric surgery.

Keywords: Obesity; Body fat distribution; Cardiovascular risk factors; Obesity treatment.

Introduction

The prevalence of obesity has increased dramatically worldwide, about 60% in Europe in the last 15 years and 50% in USA in the last 10 years.[1–4] This increase has a major impact on public health, because obesity is a known risk factor for metabolic and cardiovascular diseases such as type 2 diabetes, dyslipidemia, hypertension and coronary heart disease, and a major cause of mortality. Indeed, health-care costs of obesity-associated diseases increased to $ 51.6 billion in 1995, approximately 5.7% of all health-care expenditures in the United States.[5] An increased annual cost of care related to increased Body Mass Index (BMI) has also been seen. In addition, more than $ 30 billion per year are spent on weight-reduction programs.

Unfortunately the efficacy of obesity treatments did not increase accordingly. The standard conservative treatments of obesity (diet, physical activity, cognitive-behavioural therapy and drugs) are effective in the short term, but ineffective in the long-term in 95% of patients. A recent survey found that within one year after diet alone approximately 75% of subjects regained most of their weight. The addition of behavioural treatments modestly improved the results. However, even after a combined behavioural modification and diet programme, participants regained 60% of the lost weight within 1 year.[6–11] Bariatric surgery is, actually, the only treatment that achieves a sufficient and durable weight loss.[12]

The recurrent inefficacy of obesity treatments in producing maintained weight loss is partially due to the unrealistic expectations of patients attending an obesity clinic, since these patients are often seeking a cosmetic result.[13–14] On the contrary, the target of weight loss treatment of the World Health Organisation (WHO), 5–10% of the initial weight, is intended to bring about a significant reduction of cardiovascular and metabolic risk factors and also of mortality risk.[15]

The evidence-based medical guidelines have clearly identified the beneficial health effects of modest weight loss, especially in patients having cardiovascular and metabolic complications. A large proportion of obese patients with type 2 diabetes, hypertension, dyslipidemia or coronary diseases, improves glycemic control, reduces blood pressure, and reduces cholesterol levels respectively, even after a weight loss of 10% or less.

The identification of overweight or obese patients at high risk of coronary heart and/or peripheral arterial disease is a primary endpoint, because the obesity treatment can significantly reduce their risks and can have a substantial effect on morbidity and mortality.

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Abdominal obesity and cardiovascular diseases

Obesity is recognized as an independent risk factor for metabolic and cardiovascular diseases. However, patients having severe obesity can display a normal metabolic profile with no signs of cardiovascular disease. On the contrary, any modestly overweight patient (BMI $< 30\ kg/m^2$) can suffer from several metabolic cardiovascular diseases irrespective of the degree of obesity. In other words, the BMI is not the best parameter to identify patients at risk.[16–18]

The risk of comorbidity development depends on the severity of obesity, but more on body composition and fat mass distribution. The major risk of cardiovascular and metabolic diseases is linked to abdominal repartition of fat, and chiefly to visceral localization of adipose tissue (Fig. 1).[19–20] The visceral adipocytes are responsible for the production and secretion of many adipokines. These hormones induce important metabolic modifications (insulin resistance, glucose tolerance, lipid profile) while also producing pro-atherogenic effects (endothelial dysfunction, increase of inflammations markers). These changes are accountable for an increased risk of atherogenic dyslipidemia, type 2 diabetes, hypertension, atherosclerosis, thrombosis and inflammation (Fig. 2).[21–23] Waist

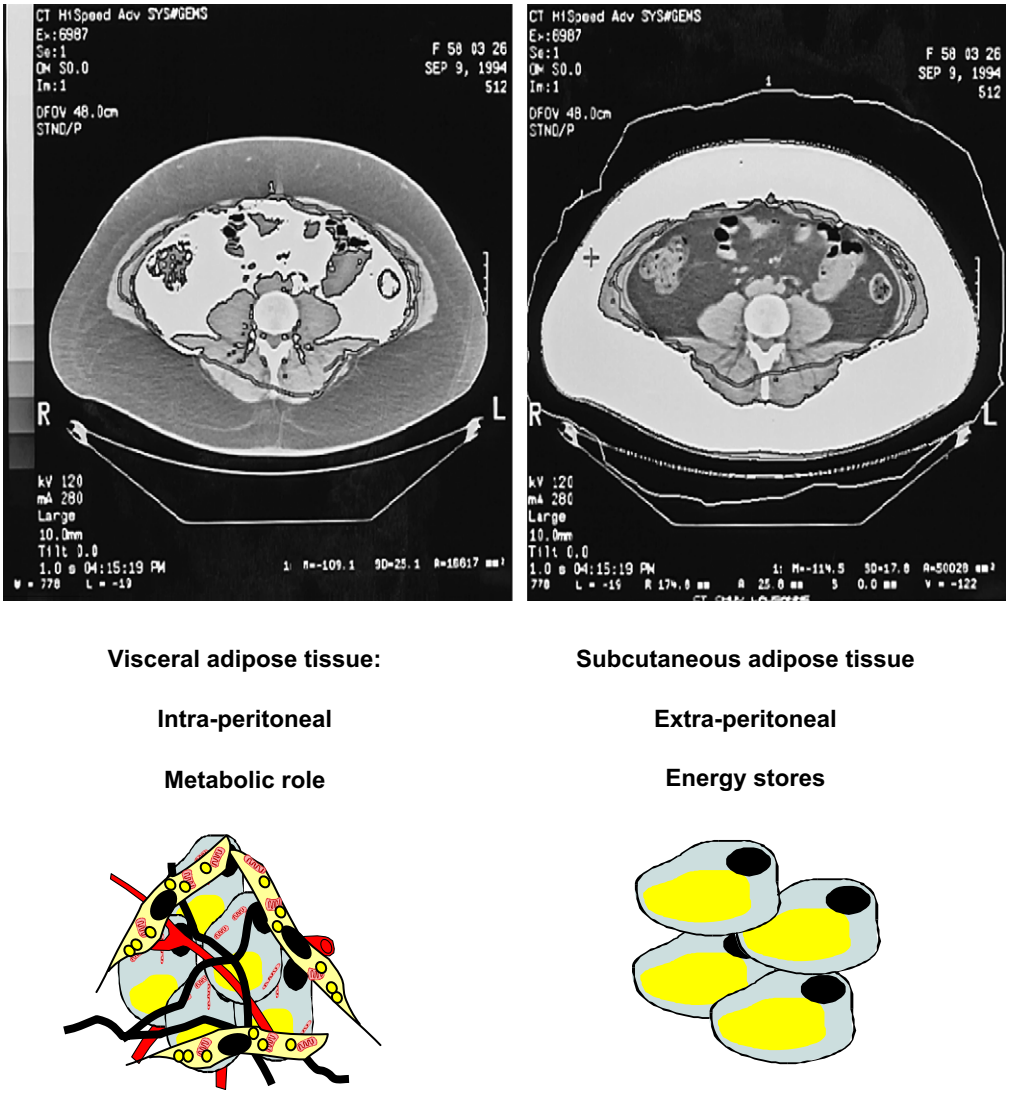

Fig. 1. This CT scan performed at the abdominal level to show the distribution of the visceral and subcutaneous adipose tissue. There are very important differences in morphology, physiology, metabolic activity and hormonal sensitivity between the two compartments. The visceral adipose tissue compartment has especially a metabolic role, while the abdominal subcutaneous compartment has rather a function of energy store.

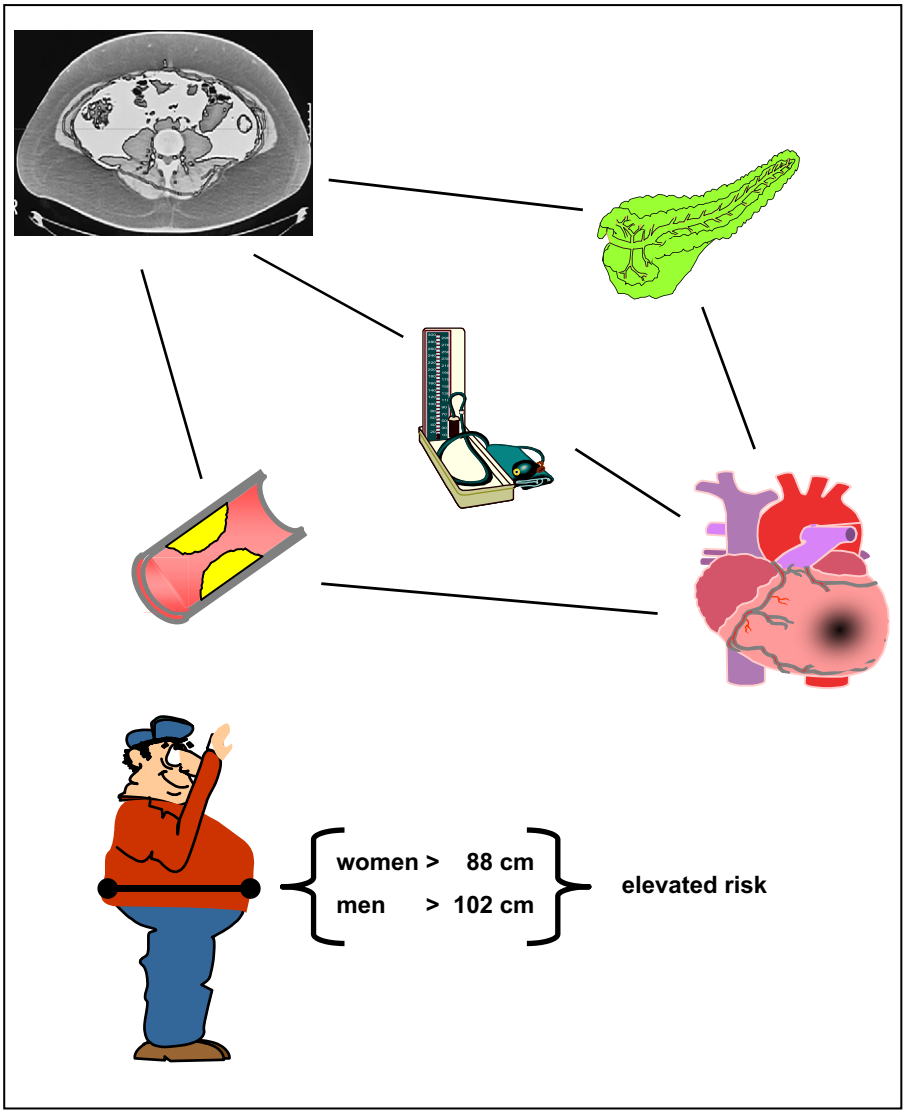

Fig. 2. The abdominal distribution of fat mass is an independent risk factor for cardiovascular and metabolic diseases. This risk is especially elevated when waist circumference is above 88 and 102 cm respectively in women and men.

circumference is a good parameter for the evaluation of body fat distribution and of cardiovascular and metabolic risk factors.[24]

In conclusion, obesity, evaluated by BMI, and abdominal distribution of adipose tissue, evaluated by waist circumference, are two major risk factors for cardiovascular and metabolic diseases.

Obesity treatments

Diet

For the last few decades, diet has been the most common treatment used to induce weight loss and it is still frequently used. Patients seeking weight loss have many diet options: low fat, low carbohydrate, high protein and low calorie. In spite of a wide use of nutritional restriction, very few data are available concerning effectiveness and safety of these diets in the long-term. Prospective and randomised studies evaluating the results of diets in the long-term are rare. Recently, Dansinger *et al.*, have compared the efficacy of four types of diet during 12 months of treatment.[25] In this study the weight loss was between 2.1% and 3.2% of initial weight. Moreover, the decrease of weight was maximal at 2 months, followed by a subsequent rise with an upward trend at the end of study. Interestingly, even during the first month the adherence to the diet was $< 70\%$ and by 6 months was $< 30\%$. Compliance was independent of diet type.

Drugs

Pharmacological treatment provides valid support for management of obesity, combined with diet and/or behavioural therapy. Drugs are retained for patients having a BMI $> 30\ kg/m^2$ or an increased weight associated with metabolic or cardiovascular diseases. The results of pharmacological treatment are approximately equivalent for all drug.[26,27] The mean weight loss is 6–10% of initial body weight after 1 year, with a fast and significant decrease of weight during the first 6 months, a subsequent rise and a final stabilisation (Table 1). If the treatment is discontinued weight gain is common. This situation facilitates weight cycling syndrome, thus increasing cardiovascular and metabolic risk. The drug treatment should ideally be continued and not stopped, just as all drug therapies for chronic diseases. The aim of drug use is to contribute towards a moderate weight loss in association with long-term dietetic and behavioural measures, with the final objective of improving metabolic and cardiovascular profile.

Currently, only two drugs are approved by the FDA for long-term treatment of obesity: orlistat and sibutramine. These are recognized to be safe and moderately effective for weight loss and reduction of cardiovascular and metabolic risk factors. Other drugs, with anorexiant effects (phenylpropanolamine, fenfluramine, dexfenfluramine) are associated with increased prevalence of cardiac valvulopathy and risk of hemorrhagic stroke and therefore recently have been withdrawn from the market.

Orlistat prevents the absorption of 30% of dietary fat via inhibition of lipase activity.[28] Orlistat is minimally absorbed (< 1%) and so has no systemic effects. Systematic reviews show that orlistat produces a weight loss of 9 to 10% compared with a 4 to 6% in placebo group.[29,30] The daily dose of 120 mg three times per day causes gastrointestinal adverse effects, as well as increased defecation, oily evacuation, fecal urgency, in at least 10% of patients. Nevertheless, these effects decrease with reduction of dietary fat intake. Orlistat also induces a significant reduction of serum cholesterol and improves glucose tolerance, independently of weight loss.[31–34]

Table 1. Pharmacological treatment consents a moderate weight loss (5–10% initial body weight), equivalent for all drugs, enough to reduce cardiovascular and metabolic risk factors associated with obesity, but not sufficient to be satisfy patient expectations, that habitually are more than 20% of initial weight

Drug	Weight loss
Orlistat	6–8%
Sibutramine	7–9%
Rimonabant	7–8%

Sibutramine is a serotonin and norepinephrine reuptake inhibitor, that acts as an appetite suppressant and increases thermogenesis.[35] The daily dose of 10 mg is effective to obtain a weight loss of 7 to 9% when associated to behavioural therapy.[36,37] This result is short-lived if treatment is discontinued.[38] Sibutramine improves also lipid profile and glucose control, with a reduction of cardiovascular risk factors.[39] The most common adverse events are increased in blood pressure and heart rate. These effects are dose-related and sometimes require discontinuation of the medication.[40]

Fluoxetine, an antidepressant drug, also is recognized for treatment of obsessive compulsive disorders, premenstrual dysphoric disorder and especially for eating disorders, which affect about 40% of obese patients.[41,42] Fluoxetine is unsuccessful in inducing a significant weight loss, but it reduces compulsive eating, therefore stopping the weight increase normally observed in patient with severe eating disorders. Moreover, fluoxetine is the ideal antidepressant drug for patient with an excess of body weight.

Rimonabant is a new anti-obesity drug, available in several countries in Europe but still not approved by FDA for treatment of metabolic syndrome. Rimonabant is a selective cannabinoid receptor blocker, that reduce food intake via a modulation of dopaminergic and opioid neurone activity.[43–45] In addition, via modulation of cannabinoid receptors in the adipocytes, rimonabant should be active in a variety of physiological processes, including regulation of energy balance, insulin action, lipid and glucose metabolism, angiogenesis.[46,47] Recent studies show that rimonabant is effective in producing a weight loss of 7–8% of initial weight after 1 year of treatment.[48,49] The weight reduction is especially significant during the first six months (as for orlistat and sibutramine). Discontinuation of treatment induces a fast reversion to initial weight. Rimonabant also results in significant improvement of metabolic profile with reduction of cardiovascular risk factors. In a recent study, 15% of patients treated discontinued participation (7% in placebo group). The reason for discontinuation was, for about half of these, a psychiatric disorder.[50]

Bariatric surgery

Surgery has been shown to produce effective and sustained weight loss, which in turn results in improvement in obesity related comorbidities, quality of life and survival.[51–54] Two operations are usually proposed: gastric banding and Roux-en-Y-gastric bypass (RYGBP). Gastric banding is currently the most popular purely restrictive bariatric operation in Europe and in many countries. It has a low operative morbidity, but

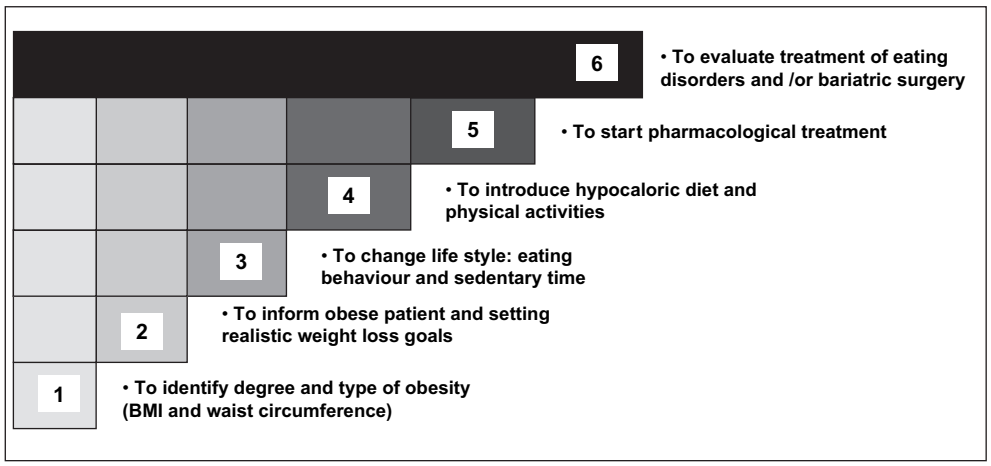

Fig. 3. Outpatient management take in several steps in according to severity of obesity and associated comorbidities and motivational readiness of patient. The management goals are modified and adapted in function of obtained results. A multidisciplinary team for management of eating disorders and/or bariatric surgery may be required.

is associated with a substantial late complication rate. RYGBP is also a restrictive procedure, but with minor intestinal malabsorption. It provides increased weight loss together with better food tolerance, but is associated with nutritional deficiencies and higher operative morbidity. Some bariatric surgeons consider Roux-en-Y gastric bypass to be the procedure of choice in the treatment of morbid obesity. The mean weight loss after RYGBP is 50 to 75% of excess weight two years postoperatively. About 75% of patients maintain this result up to four years after surgery. Importantly, cardiovascular and metabolic comorbidities are resolved or improved in most patients. Bariatric surgery imposes a rapid and drastic change in eating behavioural, body weight and shape perception, and in metabolic status, that may cause psychological and/or metabolic imbalance. Therefore, the selection, the education and the follow up of patients who undergo surgery, require a multidisciplinary team in order to decrease the preoperative risk, the prevalence of metabolic, nutritional and psychological complications. Currently, bariatric surgery is limited to patient having severe obesity or significant associated comorbidities.

Outpatient management

The first aim of obese patient management is to identify the degree and type of obesity. Two parameters are used: BMI and waist circumference. Patients having more than 30 kg/m^2 or 25 kg/^{2} with a waist circumference $>$ 88 cm for women and 102 cm for men, have a high cardiovascular and metabolic risk and specific treatment to achieve weight loss is needed.

The second step is to inform the patient of implications of excess body weight for health and then set realistic weight loss goals. In this context, a good physician-patient partnership is essential to achieve and maintain weight loss.

The third step is going into action. Changes in physical activity and food intake are crucial to produce a state of negative energy balance and obtain a weight loss. Initially, simple modifications of daily activities and a reduction of sedentary time can be helpful. Moreover, effortless changes in quality and quantity of food intake can be obtained reducing snack and soft drink consumption, sweet and fatty food use.

When excess weight is significant and/or behavioural modifications unsuccessful, the fourth step is introducing a moderate hypocaloric diet and organized physical activities.

This fourth step can be supported by the use of pharmacological treatment, which is the fifth phase of obese patient management.

The following steps, concerning eating disorders management and bariatric surgery, require a multidisciplinary approach by a team of endocrinologists, dieticians, psychiatrists and surgeons (Fig. 3).

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